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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/050,249	03/30/1998	HARUKI OKAMURA	OKAMURA=2B	6601

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EXAMINER	
JIANG, DONG	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 12/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/050,249	OKAMURA ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/29/05 & 9/28/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *93 and 95-120* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *93 and 95-120* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED OFFICE ACTION

The request filed on 29 June 2005 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/050,249 is acceptable, and a RCE has been established. An action on the RCE follows.

Applicant's amendment filed on 30 March 2005 is acknowledged and entered. Following the amendment, claim 94 is canceled, claims 93, 98-101, 104, 106 and 109 are amended.

Applicant's response (supplemental) filed on 28 September 2005 is acknowledged.

Currently, claims 93 and 95-120 are pending and under consideration.

Declaration

A. The declaration of Dr. Shizuo Akira filed on 28 September 2005 is acknowledged. It is noted that the second page of the declaration containing items 12-18 is missing. The declaration is considered to the extent of the relevant item (item 25) pointed by applicants as the rest of the items are either missing or unclear as to their relevance to the instant case since this declaration was not originally filed for this application. The declaration is insufficient to overcome the rejection of claims 93, 95, 96 and 98-118 based upon lack of written description under 35 U.S.C. 112, first paragraph, for the following reasons. Item 25 of the declaration indicates that it would have been a routine exercise to generate variants of SEQ ID NO:1 and screen for the desired inherent biological properties, namely induction of IFN-γ production by immunocompetent cells. However, the issue of the rejection is not whether generating variants and screening for said biological properties are routine or not, rather, the issue is that the specification does not describe any homologues meeting the limitations of the claims, and the skilled artisan cannot envision the detailed chemical structure of the encompassed homologues. Therefore, the specification does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. For more detail, see the rejection under "***Rejections under 35 U.S.C. 112***" below.

B. The declaration of Dr. Haruki Okamura filed on 28 September 2005 is acknowledged, and it is insufficient to overcome the prior art rejection of claims 93 and 95-120 under 35 U.S.C. 103(a) over Nakamura *et al.* (*Infect. Immun.* 61: 64-70, 1993), for the reasons addressed under "***Rejections Over Prior Art***" below.

Withdrawal of Objections and Rejections:

All objections and rejections of claim 94 are moot as the applicant has canceled the claim.

The objection of the specification is withdrawn in view of applicant's amendment.

The new matter rejection of claims 93, 95-96, 98-117 and 119 under 35 U.S.C. 112, first paragraph is withdrawn in view of applicant's amendment.

The rejection of claims 98-117 and 119 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendment.

Rejections under 35 U.S.C. 112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 93, 95, 96 and 98-118 remain rejected, and claim 119 is rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description for the reasons set forth in the previous Office Actions.

Applicants argument filed on 28 September 2005 has been fully considered, but is not deemed persuasive for reasons below.

At pages 2-5 of the response, the applicant argues that the specification provide adequate written description for a mAb specifically recognizing a "homologue" of IL-18, which must have, in addition to the homologous amino acid sequence to SEQ ID NO:2, the physicochemical properties (1)-(3) as recited in claim 93, that, citing the declaration by Dr. Akira (item 25), such homologues would have been easily obtained at the time the invention was made by applying

recombinant techniques known in the art, and that once a homologue is obtained, a monoclonal antibody thereto is also easily obtained in accordance with the disclosure of the specification. This argument is not persuasive because the issue is not how to make a functional homologue, rather, the issues are: first, said "homologue" of IL-18 reads on any functional equivalent of IL-18 without sequence similarity, and specification provides none with this regard. Further, even if such homologue could be generated, the antibody thereto would encompass those specifically recognizing both SEQ ID NO:2 and the "homologue", and those only specifically recognizing the "homologue", but not SEQ ID NO:2, and the specific sequence(s) or epitopes of the later are not described in the specification, and therefore, it does not reasonably convey to one skilled in the relavant art that the inventors, at the time the application was filed, had possession of the claimed invention. To the extent that such variants may have epitopes not found in SEQ ID NO:2, there is no written description of such epitopes, and therefore, of antibodies that bind to them.

Claims 93, 95, 96 and 98-119 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to a monoclonal antibody specifically recognizing a polypeptide of SEQ ID NO:2, wherein Xaa is Met or Thr, does not reasonably provide enablement for with claims to monoclonal antibodies to variants of SEQ ID NO:2 (as recited in claims 93, 94, 96), or any "interferon-γ inducing protein" (claim 118). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record set forth in the previous Office Actions paper No. 22, 24, 29 and 31, as the newly amended independent claim 93 closely resembles the previous version with respect to the limitation for part (ii) a variant/homologue.

The newly amended claim 93 encompasses a mAb to a "homologue" of IL-18 with "one or more amino acids replaced", which reads on a functional equivalent not necessarily having any sequence similarity to the disclosed SEQ ID NO:2. as addressed in the previous Office Actions, enablement is not commensurate in scope with claims to a mAb recognizing any or all possible functional equivalent of IL-18. It is noted that the patentability of the claimed homologue rests not on the biological property, but rather the particular sequences disclosed in

the specification as filed because there exist other distinct proteins with the same biological property. The specification merely discloses one mAb, M-1 (Example 3), which reacts specifically with SEQ ID NO:2, and does not teach how to make a commensurate number of "homologues" meeting the limitations of the claims, and how to make the full scope of the antibodies. Further, said homologue would undoubtedly possess epitopes distinct from that of SEQ ID NO:2, i.e., to the extent that the claims encompass antibodies that bind to epitopes not found in the particularly disclosed sequences, and the specification does not teach any of such epitopes, nor how to use the antibody thereto. Therefore, the structure properties of the homologue and the use of the corresponding antibodies are not predictable. The specification fails to enable the skilled artisan to make and use the full scope of the subject matter of the noted claims.

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 93 and 95-120 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Nakamura *et al.* (*Infect. Immun.* 61: 64-70, 1993), for the reasons set forth in the previous Office Actions, paper No. 22, 24, 29 and 31, and the Office Actions mailed on 11 February 2004, and 01 November 2004.

Applicants argument filed on 29 March 2005 has been fully considered, but is not deemed persuasive for reasons below.

At pages 12-15 of the response, the applicant argues that it is the examiner's hindsight reconstruction that Nakamura's factor in the serum sample was the same as IGIF found in the liver extract, and the higher molecular weight form was considered to be bound to another protein or to exist in an oligomeric form, as Nakamura's first publication never states such, that relying on Nakamura's later publication when considering the obviousness is unreasonable. This argument is not persuasive because it is *not examiner's hindsight reconstruction or reasoning*, rather, the examiner merely provides the post filing date *evidence* or *fact* showing what had already been identified and known prior to applicants filing date is the same product as that in the instant invention. MPEP 2124 indicates that in certain circumstances, references cited to show a universal fact need not be available as prior art before applicant's filing date. In re Wilson, 311 F.2d 266, 135 USPQ 442 (CCPA 1962). Such facts include the characteristics and properties of a material or a scientific truism.

At page 16 of the response, the applicant argues that Nakamura has not succeeded in obtaining a monoclonal antibody to IGIF, even after the present application was filed, and therefore the claimed invention is unobvious over Nakamura. This argument is not persuasive because, as addressed in the previous Office Actions, "in addition to conceding the obviousness of a mAb to 'the protein of claim 1,' counsel stated in the reply of 14 February 1997 that "[t]echniques of raising monoclonal antibodies are well known" and that "[k]nowing the biological activity of such protein [as the protein of claim 1], one of ordinary skill in the art would have been motivated to make a monoclonal antibody for the purpose of immunoaffinity chromatography or for the purpose of blocking its activity. The techniques for doing so are well known." Therefore, it is irrelevant whether or when Nakamura obtained the mAb.

Additionally, Applicants argument filed on 28 September 2005 (supplement) has been fully considered, but is not deemed persuasive for reasons below.

At pages 6-7 of the response, the applicant argues that, based on the declaration of Dr. Okamura (co-author of the Nakamura reference (1993), item 11), that Dr. Okamura did not expect that the factor disclosed in the Nakamura reference (1993) would be the same as the

polypeptide of the present invention. This argument is not persuasive because it is irrelevant as to what to *expect* since the *evidence* has shown that they are the same molecule.

Conclusion:

No claim is allowable.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
11/22/05